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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,300	08/21/2001	Todd Lewis Talarico	35780/233666 (5780-5)	8297

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EXAMINER

DEVI, SARVAMANGALA J N

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 12/19/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/934,300

Applicant(s)

TALARICO ET AL.

Examiner

S. Devi, Ph.D.

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 ~~is/are~~ are pending in the application.
- 4a) Of the above claim(s) 1-11 ~~is/are~~ are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-19 ~~is/are~~ are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 10/01/03 (paper no. 9) in response to the non-final Office Action mailed 07/01/03 (paper no. 8). With this, Applicants have amended the specification.

Status of Claims

2) Claims 1-11 have been canceled via the amendment filed 10/01/03.
Claims 12, 13, 15-17 and 19 have been amended via the amendment filed 10/01/03.
Claims 12-19 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the specification made in paragraph 4 of the Office Action mailed 07/01/03 (paper no. 8) is withdrawn in light of Applicants' amendment to the specification.

Objection(s) Maintained

6) The objection to the drawings made by the Draftsperson as indicated in PTO-948 attached to the Office Action mailed 07/01/03 is maintained for reasons set forth therein. A copy of the PTO-948 is supplied with this Office Action.

Rejection(s) Withdrawn

7) The rejection of claim 12 made in paragraph 5(a) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

8) The rejection of claim 13 made in paragraph 5(b) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of

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Applicants' amendment to the claim.

9) The rejection of claim 17 made in paragraph 5(g) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

10) The rejection of claim 19 made in paragraph 5(h) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

11) The rejection of claim 17 made in paragraph 5(i) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claim 16 made in paragraph 5(c) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' arguments.

13) The rejection of claim 12 made in paragraph 5(d) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' arguments.

14) The rejection of claim 12 made in paragraph 5(e) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn.

15) The rejection of claim 15 made in paragraph 5(f) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn.

16) The rejection of claims 13-19 made in paragraph 5(j) of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn.

17) The rejection of claims 12-16 and 18 made in paragraph 7 of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 102(b) as being anticipated by Talarico *et al.* (*Biochim. Biophys. Acta* 1476: 53-65, 2000), is withdrawn.

18) The rejection of claims 12, 17 and 19 made in paragraph 9 of the Office Action mailed 07/01/03 (paper no. 8) under 35 U.S.C § 103(a) as being unpatentable over Talarico *et al.* (*Biochim. Biophys. Acta* 1476: 53-65, 2000) in view of Feola *et al.* (US 5,439,882), is withdrawn.

Rejection(s) under 35 U.S.C § 103

19) Claims 12-16 and 18 are rejected under 35 U.S.C. § 102(b) as being unpatentable over Woghiren *et al.* (*Bioconj. Chem.* 4: 314-318, 1993) in view of Miles *et al.* (*Art. Cells Boold Subs. Immob. Biotech.* 25: 315-326, 1997 - Applicants' IDS) or Iwashita *et al.* (*Biomat. Art. Cells Art. Org.* 16: 271-280, 1988, already of record) or Rausch *et al.* (US 5,084,558 - Applicants' IDS) and Katsunuma *et al.* (US 4,229,571) or JP 53038617 ('617).

Woghiren *et al.* taught a method of preparing a chemically modified protein solution which involves the step of activating PEG into a stable reagent. The activated PEG was dissolved in a solvent, such as, methanol; and the solution was subjected to gel filtration for the purpose of purification. The resultant PEG solution was combined with a protein solution (see abstract; page 314, left column; and 'Experimental Procedures', especially on page 315). That the prior art gel filtration includes or involves at least one filter is implicit from the teachings of Woghiren *et al.* in light of what was well known in the art. For instance, Katsunuma *et al.*, or the JP '617 patent taught that gel filtration is effected through a filter (see claim 5 of Katsunuma *et al.* and the abstract of the '617 patent). That the process of filtering reduced the levels of contaminants in the prior art method and rendered the solution substantially free of contaminants is implicit from the teachings of Woghiren *et al.*

Woghiren *et al.* do not teach the protein solution to be a hemoglobin protein solution.

Miles *et al.* identified the need in the art for the safe use of purified hemoglobin solutions as therapeutics in humans, and taught a method of accomplishing it by linking to POE to prevent toxicity (see abstract). Miles *et al.* taught that derivatization of proteins with PEG has been shown to increase circulating half life of the protein and to decrease immunogenicity *in vivo* (see page 320).

Iwashita *et al.* taught a solution of hemoglobin which rendered stroma free by filtration using 0.22 um membranes and unltrafiltered (see 'Materials and Methods'; and pages 277 and 278).

Iwashita *et al.* taught tht chemical modification of the stroma free hemoglobin by attachment to POE is done to extend the life time of hemoglobin in the circulation (see page 278).

Rausch *et al.* disclosed a solution of endotoxin-free, stroma free hemoglobin (see Examples).

Given the identified need in the art to obtain safer therapeutics comprising purified hemoglobin solutions as taught by Miles *et al.*, it would have been *prima facie* obvious to one of

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ordinary skill in the art at the time the invention was made to replace Woghiren's protein solution with Miles' hemoglobin protein solution, Iwashita's stroma-free hemoglobin or Rausch's endotoxin-free, stroma free hemoglobin solution in Woghiren's method to produce the method of the instant invention, with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of producing a safer non-toxic hemoglobin solution for use as a therapeutic, because modification of hemoglobin solution by linking to POE was known in the art to prevent toxicity as taught by Miles *et al.* and to increase its circulating half life *in vivo* as taught by Miles *et al.*

Claims 12-16 are *prima facie* obvious over the prior art of record.

20) Claims 17 and 19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Woghiren *et al.* (*Bioconj. Chem.* 4: 314-318, 1993) as modified by Miles *et al.* (*Art. Cells Boold Subs. Immob. Biotech.* 25: 315-326, 1997 - Applicants' IDS) or Iwashita *et al.* (*Biomat. Art. Cells Art. Org.* 16: 271-280, 1988, already of record) or Rausch *et al.* (US 5,084,558 - Applicants' IDS) and Katsunuma *et al.* (US 4,229,571) or JP 53038617 ('617) as applied to claims 16 and 18 above, and further in view of Feola *et al.* (US 5,439,882, already of record).

The teachings of Woghiren *et al.* as modified by Miles *et al.* or Iwashita *et al.* or Rausch *et al.* and Katsunuma *et al.*, or the JP '617 patent are described above, which do not disclose the use of the specific filter recited in claim 17.

However, Feola *et al.* taught the use of a Posidyne 0.20 micron filter to further remove microbial contaminants from hemoglobin preparations (see Example 2).

Given the art known use of micron-sized filters to filter an organic POE solution as taught by Miles *et al.*, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use Feola's Posidyne 0.20 micron filter in Woghiren's method as modified by Miles *et al.* or Iwashita *et al.* or Rausch *et al.* and Katsunuma *et al.* or the JP '617 patent to produce the instant invention with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of further removing microbial contaminants from the prior art preparation. With regard to aseptic joining, given the therapeutic purpose for the hemoglobin solution, that the prior art method as modified by Feola *et al.* involves sterile formulation is implicit from the teachings of prior art.

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Claims 17 and 19 are *prima facie* obvious over the prior art of record.

Pertinent Prior Art

21) The prior art made of record and not relied upon currently in any of the rejections are considered pertinent to Applicants' disclosure.

- Zalipsky *et al.* (*J. Macromol. Sci. Chem.* A21: 839-845, 1984) taught the activation of PEG; dissolving PEG in CH₂Cl₂, acetone, EtOH or DMF; and filtering the dissolved PEG. That the process of filtering reduced the levels of contaminants is implicit from the teachings of Zalipsky *et al.*

- Goldstein *et al.* (US 5,478,738) disclosed the use of resin or filter in gel filtration (see column 4, lines 15 and 16).

Remarks

22) Claims 12-19 stand rejected.

23) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1 (CM1). The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which receives papers 24 hours a day and seven days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

24) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

December, 2003


S. DEVI, PH.D.
PRIMARY EXAMINER